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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/990,940	11/21/2001	Hui Tian	018781-007410US	2892

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EXAMINER	
KAUFMAN, CLAIRE M	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 10/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/990,940	Applicant(s) TIAN ET AL.	
	Examiner Claire M. Kaufman	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-55* is/are pending in the application.

4a) Of the above claim(s) *1-16,26-30 and 33-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-25,31,32 and 49-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-55* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group XI in Paper No. 10 is acknowledged. The traversal is on the ground(s) that there is not an undue burden of examination. This is not found persuasive because the search and examination would be burdensome as shown by the different classification for certain groups, such as protein *vs* nucleic acid and methods *vs* products, as well as divergent subject matter. Search also is not the same for each group. For example, searching for the nucleic acid does not require the same search as for the protein, which may appear in the literature in the absence of reference to the nucleic acid if purified from a natural source, just as the search for the nucleic acid must include search of partial nucleic acid sequences with no known or recorded corresponding amino acid protein sequence. Additionally, the burden of search for the Office has increased with multiple sequences because of the rapid introduction of new sequences to public sequence databases.

The requirement is still deemed proper and is therefore made FINAL.

The Examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction

requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the Examiner before the patent issues. See MPEP § 804.01.

Information Disclosure Statement

Reference AF, JP 2001-245666, was not considered because there was not translation or English abstract.

Claim Objections

Claims 17-25 and 49-55 are objected to for reciting a non-elected invention (SEQ ID NO:15 and 16).

Specification

The disclosure is objected to because of the following informalities: in paragraph 66 (p.14, line 25), it appears that "therefore" should be --thereof--.

Appropriate correction is required.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The attempt to incorporate subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See MPEP § 608.01(p), paragraph I, regarding incorporation by reference. The hyperlink appears on p. 3, line 12.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17, 20, 25, 51 and dependent claims 18, 19, 21-23, 31, 32, 49, 50 and 52-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 17 and 20 are unclear because 17 is drawn to a nucleic acid encoding a "G-protein coupled receptor polypeptide", while dependent claim 20 recites the nucleic acid encodes a polypeptide that has "G-protein coupled receptor activity". It is unclear what the distinction between the claims is, that is, according to the art it would appear that a G-protein coupled receptor polypeptide would by definition be required to have G-protein coupled receptor activity, though the specification does not make such a requirement.

Claims 20 and 51 are indefinite because the metes and bounds cannot be determined because of the limitation of having a "G-protein coupled receptor activity". The specification lists non-limiting examples of activities p. 14, lines 18-24 (¶ 65) and p. 13, lines 26-33 (¶ 60); but it is unclear if, for example, activities such as binding an anti-GPCR antibody or binding a ligand without signal transduction is considered an "activity".

Claims 25 is indefinite because it recites "selectively hybridizes under moderately stringent conditions". The claim appears to use two contradictory terms: "selectively hybridizes" and "moderately stringent conditions". The reasons is, the specification appears to define selectively hybridize consistently with stringent conditions as follows: a nucleic acid that "specifically hybridizes under stringent conditions" means (p. 24, lines 15-22) that the nucleic acid hybridizes "only to a particular nucleotide sequence under stringent hybridization conditions when that sequence is present in a complex mixture" (e.g., library DNA), and under "conditions

under which a probe will hybridize to its target sequence... but to no other sequence." However, under moderately stringent conditions, the nucleic acid does not need to hybridize as specifically, in that it can also hybridize to a target that is a degenerate nucleic acid (p. 25, line 8-18, ¶ 99). So under moderately stringent conditions it appears the target can be less structurally identical to the probe than if it were hybridizing under only stringent conditions. The definition of "selectively hybridizes" is at odds with the definition of "moderately stringent hybridization conditions".

Claim Rejections - 35 USC § 101/112, First Paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-25, 31, 32 and 49-55 rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are drawn to a nucleic acid encoding a protein identical to or structurally related to SEQ ID NO:18 and which is G-protein coupled receptor (GPCR) or has GPCR activity. The specification's suggestion that the instantly claimed nucleic acid encodes a G protein-coupled receptor called m346b obtained from mouse embryo with a small amount expressed in brain (¶268 and Fig. 10B) is based on PCR cloning using a human sequence to obtain related mouse sequences (¶266). Utility rests (¶264) on the homology of the apparent human homolog called TGR346 to a neuropeptide Y receptor 2 (32% over 316 amino acids) and a NPAF and NPAFF neuropeptide receptor (31%). However, no specific function has assigned to human TGR346. Homology of about 30% is not sufficiently high for assignment of function based on related structure. While the sequence showed some structural identity to prior art sequences, the function(s) or specific identification of the encoded protein are not known. Also,

the specification reports that 3 non-functional splice variants of TGR346 were identified (¶ 265). Marchese et al., TIPS 20:370 (1999), describes hundreds of GPRCs found and the complexity of assigning function based on structure (*e.g.*, p. 371 col. 1 and 2, last paragraphs). m346b is apparently an orphan GPCR with no ligand or substantial activity identified. Asserted utilities include that the protein can be used to determine its ligand, making antibodies, drug screening, and the encoding nucleic acid can be used for cell identification and making transgenic animals.

The above utilities are not specific or substantial because they are generally applicable to any receptor and there is no known particular function of the instantly claimed encoding nucleic acid. Additionally, it is not known if the nucleic acid or encoded protein are differentially expressed (*e.g.*, over- or under-expressed or mutated), and if such expression would reasonably be expected to be associated with any known disease, so the asserted utility is not specific. If the encoded protein does not have utility because neither its function nor a directly associated disease is known, then antibodies that bind the encoded protein do not utility. Because it is not known specifically what the functional properties of the polypeptide encoded by the claimed nucleic acid are or what specific properties aside from sequence (*e.g.*, differential expression) the claimed nucleic acid or protein has, the claimed invention is not supported by a substantial, specific or well established utility.

After the filing date of the original application a mouse protein 88% identical to SEQ ID NO:18 (100% identical from amino acid 52-416, sequence comparison-C attached) was cloned and analyzed by homology (Nature 420:536, Feb. 2002, and GenBank Accession No:BAC33337 or BAC34735), yet no specific function was identified. The protein was labeled "hypothetical rhodopsin-like GPCR superfamily containing protein". Neither the prior art nor post-filing art can support a substantial and specific asserted utility for the claimed encoding nucleic acid.

Claims 17-25, 31, 32 and 49-55 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The specification provides little beyond protein and nucleic acid structural data (SEQ ID NO: 18 and 17) and potential activities that are generally applicable to a G protein-coupled receptor without guidance about which specific activities one could reasonably expect the polypeptide or encoding nucleic acid to possess. For the reasons above, it would require undue experimentation to use the claimed invention

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional applications do not disclose the sequence of SEQ ID NO:17 or 18 of the instant application. As a result, the effective filing date of the instant application is November 21, 2001. Furthermore, even if the claimed sequences were disclosed, the provisional applications upon which priority is claimed fail to provide adequate support under 35 U.S.C. 112, first paragraph, for claims 17-25, 31, 32 and 49-55 of this application. Because the instant application does not meet the requirements of 35 USC § 112, first paragraph, for those reasons given above, the provisional applications also do not meet those requirements and, therefore, is unavailable for benefit of priority under 35 UCS § 119(e).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17, 19, 23-25, 31, 32, 49 and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by WO200022131 (AM, cited by Applicants).

WO200022131 teaches human G protein coupled receptor hRUP4 (SEQ ID NO:128) and encoding nucleic acid (SEQ ID NO: 127). This "GPCR" that meets the definition of greater than 95% identical (see attached sequence comparison-A) to SEQ ID NO:18 of the instant application because according to the instant specification, identity does not need to be measure relative to the full-length of SEQ ID NO:18 (see ¶ 91 of the instant application, which states that "Preferably,

the identity exists over a region that is at least 25 amino acids or nucleotides in length...", p. 22, lines 12-13). Because of the large regions of identity between the prior art hRUP4 and SEQ ID NO:18 of the instant application the artisan of ordinary skill would have reasonably expected the encoded hRUP4 to be specifically bound by a polyclonal antibody generated against SEQ ID NO:18 of the instant application. Again, because of the high identity, a nucleic acid encoding hRUP4 would have been reasonably expected to be amplified by primers that specifically hybridize under stringent hybridization conditions to SEQ ID NO:17 and would have itself hybridized under stringent conditions to SEQ ID NO:17. WO200022131 also teaches part of SEQ ID NO:127 in the pCRII-TOPO vector (p. 27, line 18) as well as host cell expression (p. 41, line 17, through p. 42, line 8).

Claims 17, 20, 25, 31, 32, 49 and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by Rose et al. (J. Biol. Chem. 270(39):22661, Sept. 29, 1995).

Rose et al. teach a nucleic acid encoding a human type 2 neuropeptide Y receptor (Fig. 2) with a GPCR activity (Fig. 5). The nucleic acid is also taught in a pcDNA3 vector cloned into CHO cells (p. 2261, col. 2 second to last ¶). This GPCR meets the definition of greater than 95% identical (see attached sequence comparision) to SEQ ID NO:18 of the instant application because according to the instant specification, identity does not need to be measure relative to the full-length of SEQ ID NO:18 (see ¶ 91 of the instant application, which states that "Preferably, the identity exists over a region that is at least 25 amino acids or nucleotides in length...", p. 22, lines 12-13). Note that this is *not* a limiting definition and does not exclude 95% identity over 6 amino acids (see sequence comparison-B)

Prior Art

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. References WO200031258 (cited by Applicant) is cumulative with the WO200022131 reference above, teaching a nearly identical "GPCR" and encoding nucleic acid of hRUP4 (SEQ ID NO:37 and 38, sequence comparision-D). Gerald et al. (J. Biol. Chem. 270(39):226758, Sept. 29, 1995) is cumulative with Rose et al. cited above for disclosing the same protein and nucleic acid in a vector and host cell.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (703) 305-5791. Dr. Kaufman can generally be reached Monday through Thursday from 8:30AM to 12:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (703) 308-6564.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the examiner at the telephone number above before facsimile transmission.

Claire M. Kaufman, Ph.D.

Patent Examiner, Art Unit 1646

October 7, 2003